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07/852,390	03/16/92	WILSON	R CARPR-0022C2

EXAMINER
GUZO, D

18N2/0611

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ART UNIT	PAPER NUMBER
1805	10

DATE MAILED: 06/11/93

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☑ Responsive to communication filed on 03/15/93 ☑ This action is made final.

A shortened statutory period for response to this action is set to expire Three (3) month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☑ Claims 39-60 are pending in the application.
   Of the above, claims 48 and 49 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 39-47 and 50-60 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

This application contains claims 48 and 49 drawn to an invention non-elected with traverse in Paper No. 6. A complete response to the final rejection must include cancellation of non-elected claims or other appropriate action (37 C.F.R. § 1.144) M.P.E.P. § 821.01.

Claims 48 and 49 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 6.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order

for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 39-47, 50, 51 and 55 are rejected under 35 U.S.C. § 103 as being unpatentable over Sanders et al. in view of Alberts et al. or Watson et al.

Claims 52-54 and 56-60 are rejected under 35 U.S.C. § 103 as being unpatentable over Sanders et al. in view of Alberts et al. or Watson et al. all in view of Axel et al.

These rejections are maintained essentially for reasons of record in the prior Office Action. The rejections are grouped together here because the issues embraced by both rejections are similar and applicants arguments are applicable to both rejections.

Applicants traverse these rejections by asserting that Sanders et al. did not disclose the GS gene, that Sanders et al. only recited a large DNA fragment which may or may not have contained part of the GS gene and that applicants were the first to actually clone and sequence the GS gene. Applicants also assert that Sanders et al. teaches away from the instant invention in that since the GS gene is endogenous in host cells, amplification of the GS gene would prevent selection of transformants containing exogenous genes. Applicants further assert that no motivation could be found in the cited references for use of the GS gene in coamplifying an additional gene of interest and that the Watson et al. and Alberts et al. references provide only general teachings with no references to the GS gene

or use of said gene in coamplification of additional genes. With regard to the Axel et al. reference applicants assert that said reference indicates that the selectable marker used in coamplification should be a gene not normally expressed in the host cell. Since the endogenous GS gene is used as a selectable marker in the instant application, applicants assert that the invention is non-obvious in view of Axel et al.

Applicant's arguments filed 03/15/93 have been fully considered but they are not deemed to be persuasive.

First, with regard to the rejection of Claims 39-47, 50, 51 and 55, it is noted that said claims deal only with the cloning of the GS gene and its expression in a recombinant vector. Said claims do not recite use of the GS gene in a coamplification procedure or to endow a cell line with the ability to survive in a medium lacking glutamine, etc. Therefore, the appropriate question to be asked here is: Would an ordinary skilled artisan, seeking to clone, sequence and express a gene involved in the metabolically important conversion of glutamate and ammonia to glutamine have been motivated to do so given the teachings by Sanders et al. on procedures which were used to isolate at least part of the hampster GS gene and procedures for cloning and expression of practically any gene of interest (Watson et al. and Alberts et al.)? Given that Sanders et al. teaches a procedure which resulted in cloning "at least part of the GS-coding region." (Sanders et al., page 69, right column, 2nd paragraph)

and Alberts et al. and Watson et al. review the well known techniques used to isolate, clone, sequence and express a given gene of interest, it must be considered that the skilled artisan would have been motivated to isolate this metabolocally important gene (by standard art recognized techniques) and essentially complete the studies begun by Sanders et al. It must be considered that it would have been an obvious step to isolate and sequence the partially identified GS gene and furthermore, said isolation procedures were so well known in the art at the time of filing of the priority document of this application that said procedures would have been obvious to succeed.

It is noted that applicants claims reciting vectors comprising the GS gene and another gene linked so as to result in the amplification of the non-GS coding sequence and claims wherein host cells lacking GS activity are endowed with the ability to survive in a medium lacking glutamate by transformation of said cells with a vector containing the GS gene were rejected over Sanders et al. in view of Watson et al. or Alberts et al. all in view of Axel et al. The Axel et al. reference provided the teachings as to the coamplification of two different linked or unlinked genes wherein one DNA is an amplifiable gene coding for a dominant selectable marker such as drug resistance and the second DNA codes for a protein of interest. With regard to the application of the Axel et al. reference, applicants assert that Axel et al. only disclose use

of exogenous genes as selectable markers while applicants use the endogenous GS gene as a selectable marker and that selection of transformants comprising the GS gene would not be practical.

While the Examiner agrees that Axel et al. recites use of exogenous amplifiable genes as selectable phenotypic markers, applicants attention is directed to Axel et al.'s broad definition of selectable phenotypes: "Selectable phenotype is a phenotype which confers upon an organism ability to exist under conditions which kill off all organism not possessing the phenotype. Examples include drug resistance or the ability to synthesize some molecule necessary to cell metabolism in a given growth medium." (Axel et al., Column 4, lines 35-45). Given the aforementioned definition, the GS gene must certainly qualify as a suitable selectable phenotypic marker since said gene is an amplifiable gene coding for a dominant selectable phenotype associated with resistance to the drug methionine sulphoximine. Indeed, applicants have not disclosed any specific scientific reasons why the GS gene would not function in the method disclosed by Axel et al. or why the GS gene would not be included in Axel et al.'s broad definition of selectable phenotypic markers.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention.

This rejection is maintained essentially for reasons of record in the prior Office Action.

Applicants have apparently not traversed this rejection but instead request that the Examiner hold this rejection in abeyance until allowability of the instant claims is indicated. It is not however within the Examiner's prerogative to hold any rejection in abeyance and unless applicants provide written assurance that a deposit will be made or that a deposit of the requisite biological materials has in fact been made and a Deposit Declaration received by this Office, this rejection will be repeated.

Claims 53 and 54 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 39 and 40 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to a hampster GS gene. See M.P.E.P. §§ 706.03(n) and 706.03(z).

Claims 57 and 59 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited CHO-KI myeloma cells. See M.P.E.P. §§ 706.03(n) and 706.03(z).

These rejections are maintained essentially for reasons of record in the prior Office Action.

Applicants traverse this rejection by asserting that the skilled artisan would only need to perform routine experimentation to isolate any other mammalian GS gene or develope a myeloma cell line from any animal species and cite the Watson et al. and Alberts et al. references (cited by the examiner in the above 35 USC 103 rejection of claims 39-47 and 50-60) as evidence of the state of the prior art with regard to molecular biology at the time of filing of the instant application.

Applicants arguments are not deemed persuasive. It is unclear how the applicants can assert that only routine experimentation would be involved in development of myeloma cell lines from any mammalian species (i.e. a lemur, elephant, snow leopard, caribou, etc.) including those species for which no cell lines of any type currently exist, in identification of the GS genes from said cell lines, in generation of and selection of mutants deficient in GS activity, etc. Given that applicants present no teachings on isolation of GS genes from any other mammalian species, provide no teachings on the degree of homology between GS genes from different mammalian species, provide no

teachings on development of myeloma cell lines (from any and/or all mammals) which can be used to identify and isolate GS mutants, etc. and given that enablement of the full scope of the instant claims would involve numerous new scientific discoveries, it must be considered that undue and excessive experimentation would be involved in order to enable the instant claims. Applicants citation of Watson et al. and Alberts et al. as an indication of the state of the prior art does not specifically address the issues raised in the above rejection.

Claim 44 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is maintained essentially for reasons of record in the prior Office Action. However, the meaning of the phrase "mammalian species" has been adequately explained by applicants in the instant amendment.

Applicants traverse this rejection by asserting that the phrase "high stringency conditions" is well known to those skilled in the art and is described in many research articles. Applicants also indicate that the phrase "a part thereof from a different species" refers to either the full sequence or a part thereof of the GS gene from any mammalian species.

Applicants arguments are not deemed persuasive. The phrase "high stringency conditions" has potentially several different meanings. High stringency conditions can encompass differing levels of formamide concentrations, different hybridization temperatures, different salt concentrations, different rinse conditions, etc. Since applicants have not described the specific high stringency conditions used in the instant application, the Examiner cannot ascertain the metes and bounds of the instant claim. With regard to the phrase "a part thereof from a different species" applicants assertion that the claim reads on the entire GS gene or any part of said gene is vague in that the claim can potentailly read on anything from the entire sequence of the GS gene to a single nucleotide of said gene. Since the metes and bounds of the instant claim language cannot be determined from an examination of the claims or specification, it must be considered that the instant claim language is indefinite.

It is noted that applicants amendment has obviated the 35 USC 101 rejection of Claims 47 and 56 as well as the 35 USC 112, 2nd paragraph rejection of Claims 56-59.

No claims are currently allowable in this application.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication should be directed to Examiner David Guzo at telephone number (703) 308-1906.

David Guzo

June 8, 1993

RICHARD A. SCHWARTZ
SUPERVISORY PATENT EXAMINER
ART UNIT 185